Claims 25-49 stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Regarding claim 25, the Examiner asserts that the recitation "in turn" is vague and indefinite. The recitation "in turn" has been deleted from claim 25. Regarding claim 33, the Examiner asserts that the recitations "for providing" and "in turn" are vague and indefinite. The recitation "in turn" has been deleted and the recitation "for providing" has been replaced with "for producing". Regarding claim 39, the Examiner asserts that the recitation "treated in an after glow" is vague and indefinite. The term "after-glow" has been replaced with the term "acid flow". Support for the amendment to claim 39 is found on page 6, line 5 of the present specification. Regarding claim 42, the Examiner asserts that the recitation "suitable for allowing investigation" is vague and indefinite. The term "allowing investigation" in the above recitation has been replaced with "investigating and sensing surface interactions". Support for the amendment to claim 42 is found on page 1, lines 13-14 of the present specification. Regarding claim 46, the Examiner asserts that the recitations "is chosen" and "its specificity" are vague and indefinite. The recitation "is chosen" has been replaced with the recitation "having both" and the word "its" in the recitation "its specificity" has been deleted. The Applicants believe that the above amendments to claims 25, 33, 39, 42 and 46 overcome the Examiner's indefiniteness rejections. Reconsideration of these rejections is respectfully requested.

Claims 25-34, 37-40, 44, 45 and 48 stand rejected under 35 U.S.C. § 103(a) for obviousness over European Patent Application No. 0 104 608 to Dunn et al. (hereinafter "Dunn") in view of U.S. Patent No. 5,627,079 to Gardella et al. (hereinafter "Gardella"). Claim 35 stands rejected under 35 U.S.C. § 103(a) for obviousness over Dunn in view of Gardella and further in view of U.S. Patent No. 5,723,219 to Kolluri et al. (hereinafter "Kolluri"). Claim 36 stands rejected under 35 U.S.C. § 103(a) for obviousness over Dunn in view of Gardella and further in view of U.S. Patent No. 5,932,296 to Sluka et al. (hereinafter

"Sluka"). Claims 41-43, 46 and 47 stand rejected under 35 U.S.C. § 103(a) for obviousness over Dunn in view of Gardella and further in view of U.S. Patent No. 5,991,488 to Salamon et al. (hereinafter "Salamon").

Independent claim 25 has been amended to include a plasma layer deposited "directly" onto the film of free electron metal of the substrate. Support for the deposit of the plasma layer "directly" onto the film of free electron metal (i.e., gold surface) of the substrate is a necessary condition of the invention as disclosed uniformly throughout the entire specification. Page 4, lines 7-25 of the present specification describes metal surfaces (i.e., gold surfaces) that are cleaned by an *in situ* plasma cleaning step before modification by plasma deposition. Because the gold surface has been prepared and cleaned for the very purpose of modification by a plasma deposition, it is inherent in the specification that the plasma layer is directly applied to the gold surface.

The following Examples in the specification consistently illustrate that the plasma layer <u>must</u> be "directly" deposited onto the gold surface of the substrate. In Example 1, page 5, line 8 to page 6, line 9, a gold coated glass disc is placed in a plasma reactor (page 4, line 8-9). The discs were then treated with a dynamic air plasma (page 4, lines 27-29) which is the *in situ* plasma cleaning step of the substrate before the actual modification by plasma deposition. The cleaned surface (i.e., gold coated disc) was then treated with five pulses of an acrylic acid plasma (page 6, lines 2-6). In Example 1, no other steps are identified for the purpose of modifying the surface of the gold substrate except for the cleaning step before the plasma layer is deposited onto the surface. Therefore, it is inherent in Example 1 as well as in the following Examples that the plasma layer is <u>directly</u> deposited on the gold surface of the substrate.

In Example 2, page 6, lines 11-28, the gold coated disc is placed in a plasma reactor and cleaned by a dynamic air plasma. Next, the cleaned surfaces were treated with

ten pulses of an allyl amine plasma (page 6, lines 21-23). In Example 3, page 6, line 30 to page 4, line 12, gold coated substrates were placed in a plasma reactor and cleaned by treatment with a dynamic air plasma (page 6, lines 36-38). Next, the cleaned surfaces were exposed to ten pulses of 1 second of allylamine plasma (page 7, lines 5-7). In Example 4, page 7, line 29 to page 8, line 14, gold coated substrate were placed in a plasma reactor and cleaned by treatment with a dynamic argon (i.e., inert gas) plasma (page 8, lines 1-3). Next, the substrates were exposed to ten pulses of 1 second of an allylamine plasma (page 8, lines 7-9). In example 5, page 8, lines 16-39, gold coated substrates were placed in a plasma reactor and cleaned by treatment with a dynamic air plasma (page 8, lines 22-24). Next, the substrate were exposed to five pulses of 1 second of an allylamine plasma (page 8, lines 28-31). All of the remaining examples (i.e., Examples 6-10) include the step of placing a gold coated substrate in a plasma reactor and cleaning the substrate by treatment with a dynamic air or argon plasma and subsequently exposing the substrate to either an allylamine/octadine plasma or an allylamine/diallylsulfide plasma.

As illustrated in the above Examples, support for the addition of a word "directly" to claim 25 is inherent throughout the entire specification.

In addition, claim 28 describes the plasma deposited layer arranged <u>directly</u> on the free electron metal film. This language in claim 28 parallels the language in amended claim 25, i.e., a plasma layer deposited directly on the film at free electron metal.

Independent claim 33 has been amended to include the step of arranging a layer <u>directly</u> on the gold film by plasma deposition. Support for the amendment to claim 33 is also found in claim 28 as originally filed.

The present invention is directed to a device for investigating reactions between interactive chemicals for biological species. The device includes a substrate and a plasma layer. The substrate includes a film of free electron metal that consists essentially of

gold. The plasma layer which includes sulfur is deposited directly on the film of free electron metal of the substrate.

The two primary references the Examiner cites are the Dunn and Gardella patents. Regarding the obviousness rejection of claims 25-34, 37-40, 44, 45 and 48, the Examiner asserts that Dunn teaches that the attachment and orientation of biologically active molecules can be controlled by varying the surface chemistry of a metal substrate surface by using plasma modification techniques which yield a range of surface chemistries and properties. Moreover, the Examiner asserts that Dunn teaches that the surface of the substrate is irreversibly modified by grafting specific chemical functional groups onto the surface with a plasma of suitable material such as sulfur. Further, the Examiner asserts that Dunn fails to teach the use of gold on the substrate and fails to teach the substrate being treated in an after-glow.

The Examiner combines Gardella with Dunn and asserts that Gardella teaches a method for making refunctionalized oxyfluorinated substrates. The Examiner asserts that Gardella discloses the steps of providing a non-fluorinated base metallic material, modifying the metallic material by coating with a fluorocarbon film, oxyfluorinating the modified surface of the metal substrate with a gas/vapor plasma mixture and exposing the substrate to at least one radio frequency glow discharge. Therefore, the Examiner asserts that it would have been obvious to one of ordinary skill in the art to incorporate the use of gold and the radio frequency glow discharge described in Gardella into the method for modifying the surface chemistry of the substrate described in Dunn. Applicants respectfully disagree with the Examiner.

In view of the amendments to independent claims 25 and 33, neither the Dunn nor Gardella references teaches or suggests a plasma layer deposited "directly" on the gold surface of the substrate.

The Dunn patent is directed to a method for chemically modifying a surface of organic and/or inorganic substrates for the attachment of large molecules having available functional groups, such as proteins (see page 1, lines 1-10). Further, the surface of the substrate is irreversibly modified by grafting specific chemical functional groups onto the surface with a plasma of a suitable material such as sulfur (see page 5, lines 13-20). Moreover, Dunn discloses that the surfaces to be modified can be made of inorganic materials such as non-metals, metals and metal oxide. However, the list of inorganic materials on page 8, line 27 to page 9, line 5 does not include gold. Therefore, Dunn does not disclose the treatment of a <u>gold</u> substrate with a plasma layer that comprises a sulfur.

The Gardella patent is directed to refunctionalization of oxyfluorinated surfaces which can be formed on non-fluorinated substrates having a fluorinated surface or fluorocarbon coating applied by gas phase surface fluorination or plasma deposition. The oxyfluorinated surfaces can be refunctionalized by bonding organosilanes, isothiocyanate-containing fluorescent compounds and proteins, such as enzymes, antibodies and peptides directly to such surfaces (see Abstract). Moreover, Gardella discloses that non-fluorinated base materials or substrates, such as gold, may be used. However, the surface of the non-fluorinated substrate <u>must</u> be modified by fluorination or by coating with a fluorocarbon film (see column 6, lines 53-62). In other words, the non-fluorinated substrate must first be treated by adding a fluorine or fluorocarbon coating in the form of films to the gold substrate before depositing a plasma layer. Therefore, the Gardella patent does not disclose treatment of a gas plasma layer deposited <u>directly</u> onto the non-fluorinated gold substrate.

In view of the above, there is no motivation or suggestion in the two primary references to deposit a gas plasma layer directly onto either a gold substrate or a substrate having a gold film. Therefore, reconsideration of the above rejection of claims 25-34, 37-40, 44, 45 and 48 is respectfully requested.

Regarding the obviousness rejection of claim 35 over Dunn in view of Gardella and further in view of Kolluri, the Examiner relies on Kolluri for the teaching of the use of a gas monomer in plasma polymerization techniques. Claim 35 depends directly from claim 33 and is allowable over the teachings of Dunn and Gardella for the reasons discussed above. Therefore, the subject matter of claim 35 is believed to be distinguished over these combined teachings, as combined in the manner suggested by the Examiner, for substantially the same reasons discussed above in connection with claims 25 and 33.

Regarding the obviousness rejection of claim 36 over Dunn in view of Gardella and further in view of Sluka, the Examiner relies on Sluka for the teaching of the step of cleaning the substrate by means of a pulse argon plasma before the application of the functional groups to the substrate. Claim 36 depends directly from claim 33 and is allowable over the teachings of Dunn and Gardella for the reasons discussed above. Therefore, the subject matter of claim 36 is believed to distinguish over these combined teachings, as combined in the manner suggested by the Examiner, for substantially the same reasons discussed above in connection with claims 25 and 33.

Regarding the obviousness rejection of claims 41-43, 46 and 47 over Dunn in view of Gardella and further in view of Salamon, the Examiner relies on Salamon for the teaching of a surface plasmon resonance spectroscopy. Claims 41-43, 46 and 47 depend either directly or indirectly from claim 33 and are allowable over the teachings of Dunn and Gardella for the reasons discussed above. Therefore, the subject matter of claims 41-43, 46 and 47 is believed to distinguish over the combined teachings, as combined in the manner suggested by the Examiner, for substantially the same reasons as discussed above in connection with claims 25 and 33.

CONCLUSION

In view of the foregoing, Applicants believe that claims 25 and 28-48 are patentable over the prior art of record and are in condition for allowance. Reconsideration of the Examiner's rejections and allowance of claims 25 and 28-48 are respectfully requested.

Respectfully submitted,

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MARKED-UP VERSION OF CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at page 1, line 15 has been amended as follows:

To study real time surface interactions, several techniques are available, such as ellipsometry, reflectometry and surface plasmon resonance spectroscopy (SPR). These techniques have in common that they use the reflectance of light, generated by a laser, to analyze the growth or [desintegration] disintegration of a layer of, for instance, biological molecules at a surface.

Please delete the paragraph beginning at page 2, line 21 as follows:

[According to a first aspect of the present invention there is provided a device according to any of the claims 1 to 8.]

The paragraph beginning at page 2, line 24, has been amended as follows:

The device according to a first aspect of the present invention provides [a] good attachment of the plasma deposited layer, [a] good stability thereof and a device exhibiting good sensitivity, whereby the substrate is provided with a function layer, the functionality of which can be provided by groups such as amine, carboxylic acid, hydroxyl, acid chloride, isocyanate, aldehyde, anhydride, epoxide, and thiol groups, for example.

The paragraph beginning at page 2, line 32, has been amended as follows:

[According to a] A second aspect of the present invention[, there is provided] provides a process [according to any of the claims 9 to 19] for providing the device [according to] of the present invention.

The paragraph beginning at page 3, line 7, has been amended as follows:

In contrast to processes for providing sensor devices[,] wherein layers are arranged on a [substract] substrate by wet chemical processes which are often [time consuming] time-consuming, difficult to carry out, and often result in undesirably thick layers exhibiting a subsequent lack of sensitivity if a great deal of care [in] is not applied, the process according to the present invention is extremely flexible to work, [and] easy to effect, and offers a good cost efficiency.

The paragraph beginning at page 4, line 34, has been amended as follows:

According to a further aspect of the present invention, there is provided a process for investigating the interaction of chemical and/or biological species, for example, real time surface interactions[, according to claims 14 or 15].

IN THE CLAIMS:

Claims 26 and 27 have been canceled.

Please amend claims 25, 28, 31, 33, 39, 42 and 46 as follows:

25. (Once Amended) A device for investigating reactions between interactive chemical or biological species, said device comprising:

a substrate; and

a plasma layer deposited directly on the substrate, wherein the substrate [in turn] comprises a film of free electron metal consisting essentially of gold, and wherein the plasma layer deposited directly on the film of free electron metal comprises sulfur.

28. (Once Amended) The device according to claim [27] 25, wherein the plasma deposited layer is arranged directly on the free electron metal film and further wherein said electron free metal is selected from the group consisting of copper, silver, and aluminum [and gold].

31. (Once Amended) The device according to claim 25, wherein the plasma layers comprise one or more compounds selected from the group consisting of [amine compounds, sulphur] sulfur-containing compounds, thiols, sulfides, disulfides and diallyl sulfide.

33. (Once Amended) A process for [providing] producing a device for investigating reactions between interactive chemical and biological species, said process comprising the steps of (a) providing a pre-selected substrate,[which] said substrate [in turn] [comprises] comprising a film of free electron metal consisting essentially of gold and (b) arranging a layer directly on the gold film by plasma deposition, [which] said layer [comprises] comprising sulfur.

39. (Once Amended) The process according to claim 37, wherein the substrate is treated in an [after-glow] <u>acid flow</u>.

42. (Once Amended) The process for providing a device according to claim 33, suitable for investigating reactions between interactive bio/chemical species by means of surface plasmon resonance spectroscopy, said process comprising the steps of:

preselecting a free electron metal substrate, which metal substrate is suitable for [allowing investigation] <u>investigating and sensing surface interactions</u> by surface plasmon resonance spectroscopy, arranging a pre-selected first functional group species on the free electron metal substrate by means of plasma deposition, which first functional group species protects the free electron metal substrate from a second functional group species whose interaction with the plasma deposited first functional group species can be investigated, thereby preventing undesirable interactions between the free electron metal substrate and the second functional group species, and which first functional group species provides a desired functionality for the second functional group species.

46. (Once Amended) A method for investigating reactions between interactive bio/chemical species, by means of surface plasmon [resins] <u>resonance</u> spectroscopy, by the device of claim 25, wherein the device comprises a pre-selected free electron metal substrate, and a pre-selected, plasma deposited layer arranged on the free electron metal substrate, which plasma deposited functional group species [is chosen for its] <u>having both</u> attachment ability to the free electron metal substrate, and [for its] specificity to

further functional group species, whereby the interaction therebetween is investigatable by means of surface plasmon resonance spectroscopy.